Citation:

Gebauer SK, West SG, Kay CD, Alaupovic P, Bagshaw D, Kris-Etherton PM. Effects of pistachios on cardiovascular disease risk factors and potential mechanisms of action: a dose-response study. *Am J Clin Nutr.* 2008 Sep;88(3):651-9.

PubMed ID: 18779280

Study Design:

Randomized Crossover Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

This randomized controlled feeding study assessed potential mechanisms that may account for the lipid and lipoprotein responses to a cholesterol-lowering diet with varying doses of pistachios.

Inclusion Criteria:

- Triacylglycerols <3.94 mmol/L
- Blood pressure <160/90 mm Hg
- Body mass index (BMI; in kg/m^2) between 21 and 35
- Fasting blood glucose ≤6.93 mmol/L
- Nonsmokers
- Good general health

Exclusion Criteria:

- Inability to comply with the study protocol
- Use of blood pressure- or cholesterol/lipid-lowering medications or substances (psyllium, fish oil, soy lecithin, and phytoestrogens)
- Being pregnant or wishing to become pregnant 6 mo before of during the study
- Lactating 6 wk before or during the study
- Having a weight loss ≥10% body weight within 6 mo before the study
- Following vegetarian or weight-loss diets
- Having any of the following conditions: stroke, diabetes, liver disease, kidney disease, or autoimmune disease.

Description of Study Protocol:

Recruitment

Recruitment methods not described.

Design

The study used a 3-period randomized crossover controlled-feeding design. A 2-wk run-in period preceded the first test diet to establish a baseline for a typical American diet. Subjects were then randomly assigned to 3 treatment diets for 4 wk each. Short compliance breaks (average 2 wk) separated diet periods.

Blinding used (if applicable)

Study personnel who measured outcome variables were blinded to the diet assignments.

Intervention (if applicable)

- Lower-fat controlled diet with no pistachios
- 1 serving/d of a pistachio diet
- 2 servings/d of a pistachio diet

Statistical Analysis

- All statistical analyses were performed by using SAS (version 9.1; Statistical Analyses System, Cary, NC).
- The natural logarithmic transformation was used on the variable BMI, and the analysis was performed using transformed values.
- The results are reported at least-squares means ± SEMs. The mixed-models procedure (PROC MIXED) in SAS was used to test the effects of diet, order, period, and their interactive effects on each outcome variable.
- Tukey-Kramer-adjusted *P* values were used to determine whether the differences in the outcome variables were significant.
- Change scores for each variable were calculated. Percentage change was calculated from baseline.
- Within-subject correlations were used to test associations between clinical variable (lipids, lipoproteins, and apolipoproteins) and mechanistic variables (CETP and SCD activity).
- PROC GLM was used to test whether the slopes of the regression lines were equal across the 3 diets.
- When that requirement was met, correlations were reported as pooled values, collapsing across the treatments and taking into account the fact that repeated measurements from each subject were not independent.

Data Collection Summary:

Timing of Measurements

Baseline and prior to and at the end of each 4 wk intervention period.

Dependent Variables

- Lipids, lipoproteins, apolipoproteins, and CETP: serum blood samples
- Insulin and glucose: plasma samples
- Plasma fatty acids

Independent Variables

- 1 serving/d of a pistachio diet (1 PD, 10% of energy from pistachios; 30% total fat; 8% saturated fatty acids, 12% monounsaturated fatty acids, and 6% polyunsaturated fatty acids
- 2 serving/d of pistachio diet (2 PD, 20% of energy from pistachios; 34% total fat, 8% saturated fatty acids, 15% monounsaturated fatty acids, and 8% polyunsaturated fatty acids
- Lower-fat diet with no pistachios (25% total fat; 8% saturated fatty acids, 9% monounsaturated fatty acids, and 5% polyunsaturated fatty acids.

Control Variables

Description of Actual Data Sample:

Initial N: Original N unclear

Attrition (final N): 28 (men n= 10, women n=18)

Age, Other relevant demographics and Anthropometrics of the 28 subjects at baseline:

Characteristic	Value (n=10 M, 18 F)
Age (y)	48±1.5(35-61)
BMI (kg/m^2)	26.8±0.7(21-34)
Total cholesterol (mmol/L)	5.5±0.1(4.1-6.8)
LDL cholesterol (mmol/L)	3.5±0.1(2.3-4.9)
HDL cholesterol (mmol/L)	1.5±0.1(1.0-2.5)
Triacylglycerol (mmol/L)	1.2±0.1(0.7-1.9)
SBP (mm Hg)	111.9±2.1(96-141)
DBP (mm Hg)	69.5±1.1(59-80)
Serum glucose (mmol/L)	5.1±0.1(4.4-6.0)
Serum insulin (uU/mL)	9.27±0.8(1-23)

Ethnicity: not described

Location: Pennsylvania State University

Summary of Results:

Key Findings

- The 2 PD decreased ($P<0.05$ compared with control diet) total cholesterol (-8%), LDL cholesterol (-11.6%), non-HDL cholesterol (-11%), apo B (-4%), apo B/apo A-1 (-4%) and plasma SCD activity (-1%)
- The 1 PD and 2 PD, respectively, elicited a dose-dependent lowering ($P<0.05$) of total cholesterol (-3% and -8%), LDL cholesterol/HDL cholesterol (-3% and -11%), and non-HDL/HDL cholesterol (-2% and -10%)

Effects of diets on lipids, lipoproteins, cholesteryl ester transfer protein (CETP), and body weight (n=28)

Diet	Baseline	Control	1 PD	2 PD
TC (mmol/L)	5.40±0.1[a]	5.41±.01[a]	5.01±0.1[b]	4.92±0.1[b]
LDL-C (mmol/L	3.43±01[a]	3.42±0.05[a]	3.08±0.1[b]	2.98±0.1[b]
VLDL-C (mmol/L)	0.53±0.04[a]	0.65±0.02[b]	0.59±0.04[a,b]	0.56±0.04[a]
HDL-C (mmol/L)	1.48±0.1[a]	1.43±0.03[a,b]	1.43±0.1[b]	1.48±0.1[a]
TG (mmol/L)	1.15±0.1[a]	1.40±0.1[b]	1.28±0.1[a,b]	1.20±0.1[a]
Non-HDL-C (mmol/L)	3.92±0.19[a]	3.98±0.19[a]	3.78±0.19[b]	3.50±0.19[b]
TC/HDL-C	3.85±0.19[a]	3.98±0.19[a]	3.78±0.19[a]	3.50±0.19[b]
LDL-C/HDL-C	2.48±0.2[a]	2.55±0.2[a]	2.38±0.2[a]	2.15±0.2[b]
Non-HDL-C/HDL-C	2.82±0.2[a]	2.98±0.2[a]	2.78±0.2[a]	2.50±0.2[b]
CETP (mg/L)	1.31±0.1	1.32±0.1	1.34±0.1	1.24±0.1
Body weight (kg)	76.8±2.6	75.6±3.4	75.5±3.4	75.5±3.4

There was a significant effect of diet ($P<0.05$) for all lipids and lipoproteins. Means in a row that do not share a common superscript letter are significantly different at $P<0.05$.

Author Conclusion:

This study showed a dose-response effect of pistachio consumption within the context of a healthy dietary pattern on CVD risk factors. These effects were observed with a low dose of pistachios (~1 serving/d).

Reviewer Comments:

Recruitment methods not described; original N unclear. Women were significantly older than men. Each dietary period lasted only 4 weeks.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes
Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	???
2.	**Was the selection of study subjects/patients free from bias?**	???
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes

3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	???
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	???

6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	???
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	???
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	???
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes

8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	???
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**	???
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	???